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Control/Tracking Number: 2009-A-108-ASM
Activity: Abstract
Current Date/Time: 4/30/2009 1:51:17 PM

ETI-204 Anti-Toxin Monoclonal Antibody Treatment of Active Anthrax Disease in Rabbits

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Abstract:

Background:

ETI-204 (Anthim) is an affinity-enhanced deimmunized humanized mAb that neutralizes anthrax toxin Protective Antigen (PA) by targeting its cell receptor-binding domain. ETI-204 is being developed for the treatment of inhalational anthrax; it was previously shown to be highly effective (when administered IV or IM) in post-exposure prophylaxis in rabbits and non-human primates. Here we present results from a study designed to evaluate the efficacy of ETI-204 administered after the onset of disease in rabbits challenged with *B. anthracis* spores. This project has been supported with federal funds from Biomedical Advanced Research and Development Authority, DHHS, in conjunction with the National Institute of Allergy and Infectious Diseases, NIH/HHS, under Contract No. HHSN272200700035C.

Methods:

Rabbits (NZW) were challenged with aerosolized *B. anthracis* (Ames) spores (targeted 200 LD_{50}). Body temperature was monitored by telemetry. Laboratory evaluations (complete blood counts, C-reactive protein, PA-ECL) were performed, and the presence of bacteremia was determined by blood culture. ETI-204 was administered as a single IV (3 different doses) injection at the onset of disease defined as a significant increase in body temperature (SIBT) or positive PA-ECL result. Control animals were treated with saline (negative control) or levofloxacin (positive control). Animals were observed for clinical signs and survival for 28 days post-challenge.

Results:

All animals were treated based upon diagnostic indicators (~50% SIBT, ~50% PA-ECL). A single IV dose of ETI-204 provided substantial protection (up to 94% survival). A statistically significant increase in survival rate ($p<0.0001$ by log-rank test) was achieved with ETI-204 doses as low as 4 mg/kg compared to animals treated with saline alone. All control animals receiving saline died. The levofloxacin group exhibited 90% survival. C-reactive protein and several other hematology parameters returned to near-normal levels by 14 days post-challenge in animals treated with an efficacious dose of ETI-204. A majority of treated animals were negative for bacteremia by 7 days post-challenge.

Conclusions:

Results of this study demonstrate that a single dose of ETI-204 is a very effective treatment of active anthrax disease in rabbits, and serve to define the efficacious dose for IV administration.

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Additional Info (Complete):

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